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| **Liver Tumors** | | |  | |
| **Benign Neoplasms** | **Pathogenesis** | **Outcomes** | | **Diagnosis/Histology** |
| ***Cavernous Hemangiomas*** |  |  | |  |
| ***Adenomas*** | * Women on oral contraceptives * Could be mistaken for carcinoma | * Not premalignant * Could rupture and cause severe abdominal pain | |  |
| **Malignant Tumors** | **Pathogenesis** | **Outcomes** | | **Diagnosis/Histology** |
| ***Hepatoblastoma***  *(children)* | * Epithelial * Mixed epithelial and mesenchymal * Chromosomal deletions |  | |  |
| ***Angiosarcoma***  *(adults)* | * Exposure to arsenic, vinyl chloride * Long latent period from exposure * Very aggressive | * Not premalignant * Could rupture and cause severe abdominal pain | |  |
| ***Primary Carcinoma of the Liver*** | * Repeated cell death and regeneration from HBV and HCV infections * Viral DNA integrates into cell genome * HBV DNA integration induces broad activation of proto oncogenes * Alfatoxins also induce genomic instability (from spoiled food)   Clinical Features: Ill-defined   * Some cases can be palpated as nodular liver * Elevated serum alpha-fetoprotein in 75% of patients with hepatocellular tumors * CT, MRI, ultrasound, hepatic angiography best for small tumor diagnosis | * Hepatocellular tumors progress until encroaches on hepatic function or metastasizes to lungs. * Death within 10 months of dx e.g. cachexia, GI bleed, liver failure, rupture of tumor leading fatal hemorrhage * Cholangiocellular CA not detected until late and death occurs within 6 months | | Gross:   * Can be focal, multifocal or diffuse * May be pale or stained because cells are well differentiated * All patterns invade vascular channels   Microscopic:   * Well differentiated to highly anaplastic * Hematogenous spread late in disease to lungs * Less frequent mets than cholangiocarcinoma |
| ***Metastatic Tumors*** | * More common than primaries * Common primaries are: breast, lung, colon * Usually multiple lesions leading to striking hepatomegaly with marked increase in weight * Lesions outgrow blood supply -> necrosis * Often absence of clinical and laboratory evidence |  | |  |

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| **Disorder** | **Inheritance** | **Defect in metabolism of bilirubin** | **Clinical course** | |
| **Unconjugated hyperbilirubinemia** | | | | |
| Crigler-Naijar syndrome, type I | Ar | Absent UGT1 activity | Fatal in neo-natal period | |
| Crigler-Naijar syndrome, type II | AD, variable penetrance | Decreased UGT1 activity | Mild, occasional kernicterus | |
| Gilbert’s syndrome | Ar | Decreased UGT1 activity | Innocuous | |
| **Conjugated hyperbilirubinemia** | | | | |
| Dubin-Johnson syndrome | Ar | Impaired biliary excretion of bilirubin | | Innocuous |
| Rotor syndrome | Ar | Impaired biliary excretion of bilirubin | | Innocuous |

**Intrahepatic Biliary Tract Diseases**

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|  | **Secondary Biliary Cirrhosis** | **Primary Billiary Cirrhosis** | **Primary Sclerosing Cholangitis** |
| **Etiology** | Extrahepatic bile duct obstruction: biliary atresia, gallstones, stricture, carcinoma of pancreatic head | Possibly autoimmune | Unknown, possibly autoimmune; 50% to 70% associated with inflammatory bowel disease |
| **Sex predilection** | None | Female to male,  6 : 1 | Female to male,  1 : 2 |
| **Symptoms and signs** | Pruritus, jaundice, malaise, dark urine, light stools, hepatosplenomegaly | Same as secondary biliary cirrhosis; insidious onset | Same as secondary biliary cirrhosis; insidious onset |
| **Laboratory findings** | Conjugated hyperbilirubinemia, increased serum alkaline phosphatase, bile acids, cholesterol | Same as secondary biliary cirrhosis, plus elevated serum IgM autoantibodies (especially M2 form of anti-mitochondrial antibody) | Same as secondary biliary cirrhosis, plus elevated serum IgM, hypergammaglobulinemia |
| **Important pathologic findings before cirrhosis develops** | Prominent bile stasis in bile ducts, bile ductular proliferation with surrounding neutrophils, portal tract edema | Dense lymphocytic infiltrate in portal tracts with granulomatous destruction of bile ducts | Periductal portal tracts fibrosis, segmental stenosis of extrahepatic and intrahepatic bile ducts |